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Scientific and General

ELECTROCARDIOGRAPHIC ABNORMALITIES IN 6,000 CASES OF RHEUMATIC FEVER*

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THE segregation of a large number of patients with rheumatic fever in a Naval Hospital afforded an unusual opportunity to observe the electrocardiographic abnormalities associated with this disease. Studies of this nature have frequently appeared in the literature.[1,2,3,4] However, it is our belief that no similar large number of patients with this disease has been studied over so short a period of time. A further point of interest in the present study is the fact that all our patients were young adults, whereas previous studies included a large preponderance of children.

MATERIAL

Over a period of approximately one and one-half years, from the latter part of 1943 to the early months of 1945, 6,000 patients with rheumatic fever were observed at this activity. All but a negligible proportion were males, ranging in age from seventeen to the middle forties. The overwhelming majority of the patients were between the ages of seventeen and twenty-five. When first observed by us they were in various stages of rheumatic activity. Relatively few were seen in the first weeks of their disease and many were not seen for several months after the inception of their illness. This probably accounts for the low incidence of electrocardiographic abnormalities observed by us as compared with those reported in the studies previously cited. The degree of activity of the rheumatic process ranged from the acute fulminating to the almost completely quiescent. As soon as possible after receipt at this activity, usually within the first twenty-four to forty-eight hours an electrocardiogram was taken on each patient. Subsequent tracings were taken as indicated, in accordance with the degree of activity of the disease, the presence of previous electrocardiographic abnormalities and the suspicion of renewed rheumatic activity. The total number of electrocardiograms thus obtained in this group of patients was 9,634. The criteria of the American Heart Association for the interpretation of electrocardiograms were fairly uniformly observed. Those interpreted as indicating deviations from the normal were reëxamined and reevaluated before inclusion in the present study. Of the total thus reviewed 898 patients were found to have changes which warranted inclusion in the present summary. Any references to the clinical findings in these patients are of a most general nature. It is hoped that a more specific correlation of the individual types of abnormality with the clinical findings may be undertaken at a future date.

DISTURBANCES OF RHYTHM

Sinus tachycardia, sinus bradycardia and sinus arrhythmia, while frequently observed, were not considered of sufficient significance to be included in the present study. The accompanying table (Table 1) lists the disturbances of rhythm found in the group under consideration. It is noted that the total incidence of premature beats was no greater than that observed by Graybiel, McFarland, Gates and Webster,[5] in a group of normal aviators in the same age group. However, these observers noted no instances of auriculo-ventricular nodal premature contractions. The occurrence of this abnormality in 18 of our patients appears therefore to be of some significance.

Auricular tachycardia, auriculo-ventricular nodal tachycardia and auricular fibrillation all of the paroxysmal type have previously been noted in the presence of acute rheumatic fever.[1] These abnormalities were observed in 7 of our patients.

The interesting type of arrhythmia known as interference dissociation, or parasystole was observed in four instances in our present series (Figures 1 and 2). Since completion of this study several additional instances of this type of abnormality have been observed. The occurrence of this type of arrhythmia, of A-V nodal premature contractions, nodal rhythm, nodal tachycardia and ventricular escape to the extent observed by us appears to indicate a heightened irritability of the auriculo-ventricular node in some cases of rheumatic fever. It will be noted that in lead 3 of Figure 1 nodal tachycardia supervened, further stressing this impression.

TABLE 1.—*Arrhythmias*

	Patients
1. Sinus Arrest	2
2. Auricular Premature Systole	18
3. Auricular Tachycardia	1
4. Auricular Fibrillation	4
5. Wandering Pace Maker	10
6. A-V Nodal Premature Systole	18
7. A-V Nodal Rhythm	1
8. A-V Nodal Tachycardia	2
9. Ventricular Escape	4
10. Retrograde Auricular Contractions	6
11. Ventricular Premature Systole	49
12. Parasystole	1

Another interesting arrhythmia encountered in six in-

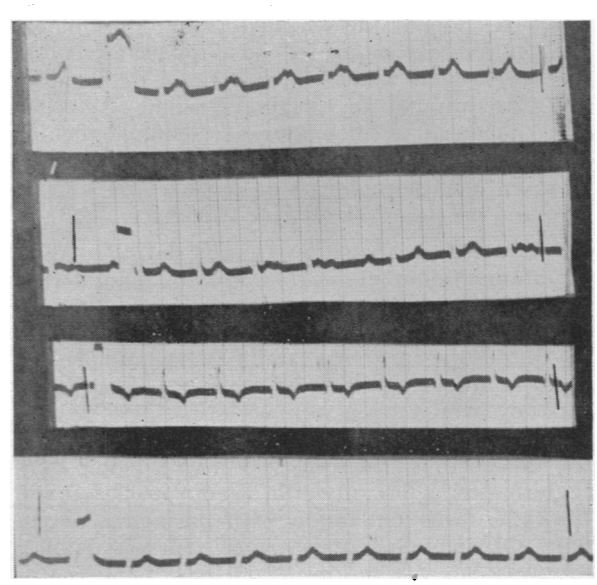

Fig. 1.—Parasystole. Nodal Tachycardia in Lead III.

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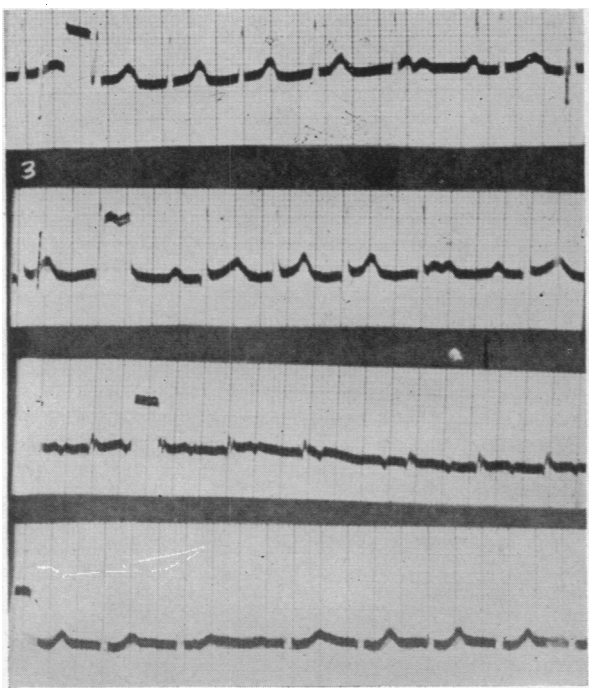

Fig. 2.—Parasystole.

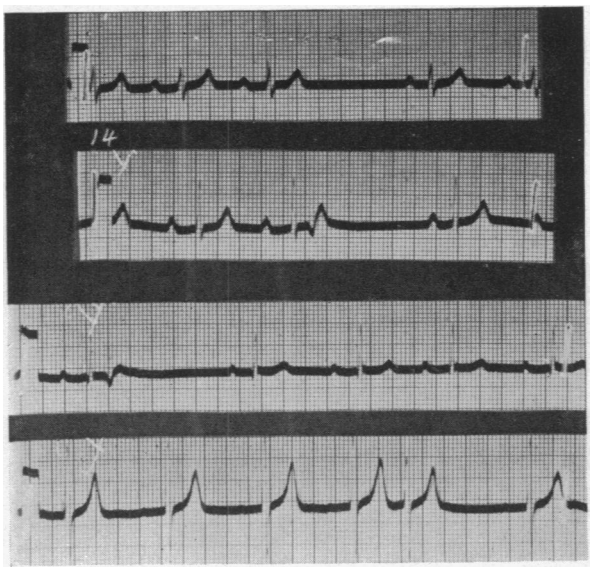

Fig. 3.—Retrograde P Waves. Followed by Dropped Beats.

stances is shown in Figures 3 and 4. This is characterized by the appearance of retrograde P waves following the usual P and QRS complexes. These retrograde P waves evidently occur at a time when the ventricle is refractory and therefore no ventricular contraction is noted to follow. This type of abnormality usually occurred in the presence of a prolonged PR interval. The occurrence of this type of disturbance may also point to increased irritability of the A-V node, with the impulse traveling in both directions after reaching the node. The auricle alone responds since the previous delay in auriculoventricular conduction has permitted the auricle to again become responsive to stimulation.

P WAVES

Changes observed in the P waves are summarized in Table 2. Only gross abnormalities were included in the

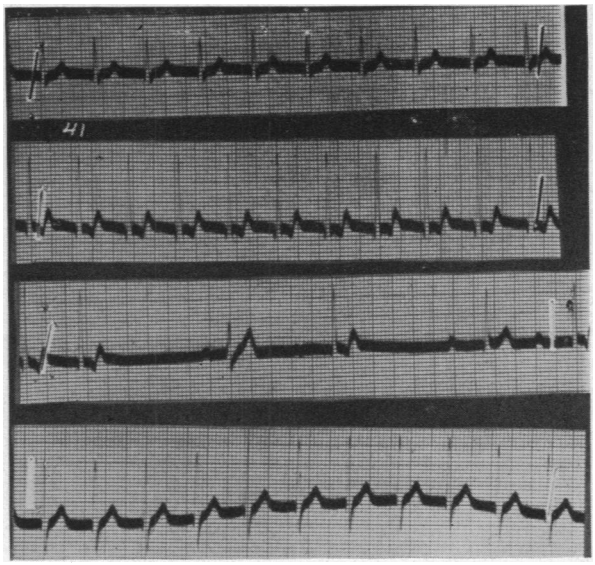

Fig. 4.—Nodal Tachycardia. Lead III shows return to basis sinus rhythm with prolonged P-R Interval, retrograde auricular contractions and dropped beats. Reversion to nodal tachycardia in Lead IV.

study. Frequent marked changes in the P waves were observed in this group in successive tracings. Inversion of the P waves in leads I and II is probably a result of a shift of the site of the pacemaker in and away from the sinoauricular node. At the termination of rheumatic activity, these inverted P waves almost invariably became

TABLE 2.—*P-Wave Changes*
98 Patients (1.63%)

Leads	High	Notched	Inverted
I	3	11	9
II	18	28	18
III	..	10	20
IV	..	12	..

upright. Significant notching or inversion of the P waves, particularly in leads I and II, and especially when associated with changes in serial tracings appears to be definite evidence of rheumatic cardiac involvement. One interesting type of P wave change observed in several instances was a progressive shift in the P waves from the upright to the inverted position in one or more leads, indicating a marked progressive shift of the pacemaker.

P-R INTERVAL

The P-R interval was determined to the nearest .02 second. Prolongation of the P-R interval has long been recognized as one of the commonest abnormalities found in rheumatic fever. As noted in Table 3, 325 patients (5.01 per cent) demonstrated this finding. Only the highest P-R interval observed in any one patient was included in the table. The vast majority of all patients in this group showed P-R intervals of .22 to .26 seconds.

TABLE 3.—*Conduction Disturbances*

Prolonged PR-Interval 325 Patients (5.01%)	Patients
1. Group with .22 to .26 sec. PR-Interval	257
2. Group with .28 to .32 sec. PR-Interval	48
3. Group with .34 to .42 sec. PR-Interval	20
4. Premature P-Waves without Ventricular Response	8
5. Wenckebach Phenomenon	4
6. Complete AV-Block	1
Other Conduction Disturbances	
1. QRS-Interval Prolonged	7
2. Left Bundle Branch Block	2
3. Right Bundle Branch Block	4
4. Wolff-Parkinson-White Syndrome	4

However, very prolonged conduction times were observed in a significant number of individuals. In successive tracings on individual patients the P-R interval varied upward and downward and often within wide limits. In most instances the P-R interval returned to normal with the cessation of rheumatic activity. However, in many cases prolonged and even markedly prolonged P-R intervals persisted throughout long periods of observation, and even after clinical and laboratory evidence of disease activity had long since disappeared. It is possible that fibrotic changes occur in the conduction system in some patients resulting in a permanent delay in A-V conduction. It certainly seems evident that mere prolongation of the P-R interval, however great, cannot be interpreted as evidence of rheumatic activity. It was at first assumed that a changing P-R interval in successive tracings was indicative of an active process in the heart. However, moderate and even marked changes in the P-R interval were noted in some instances where quiescence of rheumatic activity seemed unquestioned. Further, several patients with normal hearts and no history of recent or old rheumatic activity have been observed by us to show marked prolongation of the P-R interval with marked changes in successive tracings. It is possible that vagal influences may be responsible for these variations in A-V conduction. Recent work by Gubner, Szucs and Ungerleider[6] appears to demonstrate that vagal influences are more marked in the presence of active rheumatic fever. These investigators have shown that a large preponderance of their patients with active disease and borderline A-V conduction showed an increase in the P-R interval following the administration of prostigmine and pressure on the left carotid sinus. It is possible that the use of this latter procedure may serve as a diagnostic measure for the differentiation of the active from the inactive cases in the group with persistent prolongation of the P-R interval. However, the frequent spontaneous changes in A-V conduction noted in our patients in this group might tend to somewhat diminish the value of this procedure. We have as yet had no opportunity to investigate this problem. It seems likely, however, that the decision as to the continuance of rheumatic activity cannot be predicated upon the observation of prolonged or changing P-R interval alone. An interesting variation of the delay in A-V conduction is the progressive prolongation of the P-R interval with eventual dropped beats (Wenckebach phenomenon). This was observed in four of our patients. One such instance is illustrated in Figure 5. Complete heart block was noted in only one patient and seems to be of relatively uncommon occurrence.

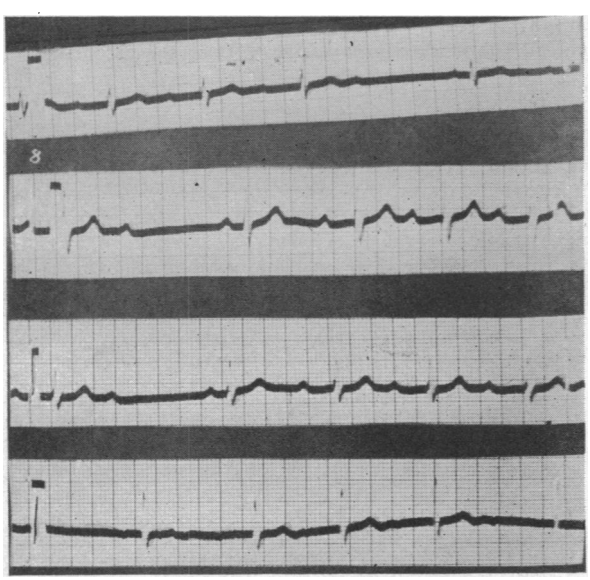

Fig. 5.—Progressive Prolongation of P-R Interval with Dropped Beats (Wenckebach Phenomenon).

OTHER CONDUCTION DISTURBANCES

Widening of the QRS complex was noted in 7 patients. This is well within the limits of normal for individuals in this age group[5] and cannot be considered of great significance. Left bundle branch block was observed in two patients and right bundle branch block in four patients (Figure 6). It is possible that the occurrence of this abnormality was purely coincidental. However, it is also possible that involvement of one or the other branch of the bundle by the rheumatic process might result in this type of abnormality. In all instances observed by us, bundle branch block persisted throughout the period of observation and long after all evidence of rheumatic activity had ceased. It is therefore not possible to determine whether the occurrence of bundle branch block in these patients was due to rheumatic involvement.

The syndrome of short P-R interval with wide QRS as observed by Wolff, Parkinson and White[7] was noted in four patients in the group under study. Two of these are shown in Figures 7 and 8. Several additional cases of this type were noted since termination of this study. This interesting abnormality is believed to be due to passage of the conduction impulse through a congenital aberrant conduction bundle between one auricle and ventricle. Its occurrence in rheumatic fever may be purely coincidental. However, recent investigations suggest grounds for speculation as to its specific importance when observed in rheumatic fever patients. It has been shown that digitalis and cholinergic drugs, due to their depressant action on the A-V node have the ability to produce this abnormality in individuals who have this type of congenital bundle.[8] In such cases the aberrant bundle, being unaffected or less affected by these drugs continues to function and reproduces the abnormal pattern. This

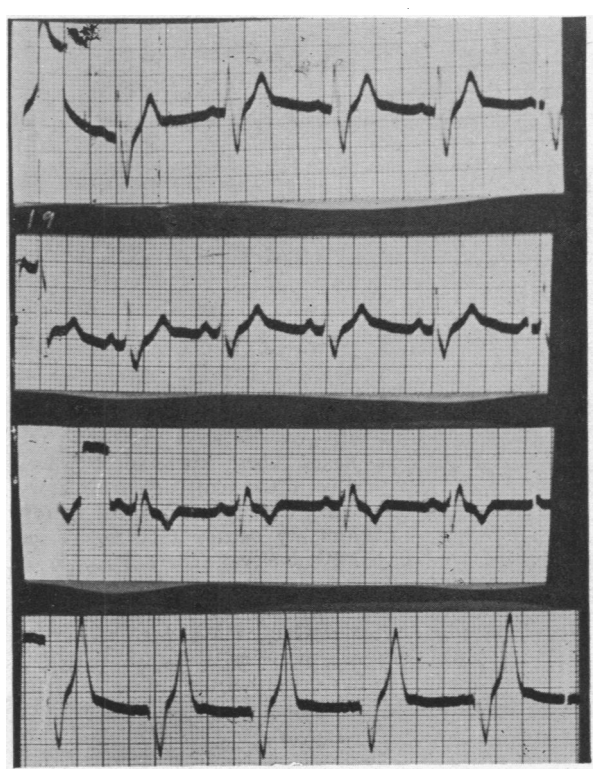

Fig. 6.—Right Bundle Branch Block.

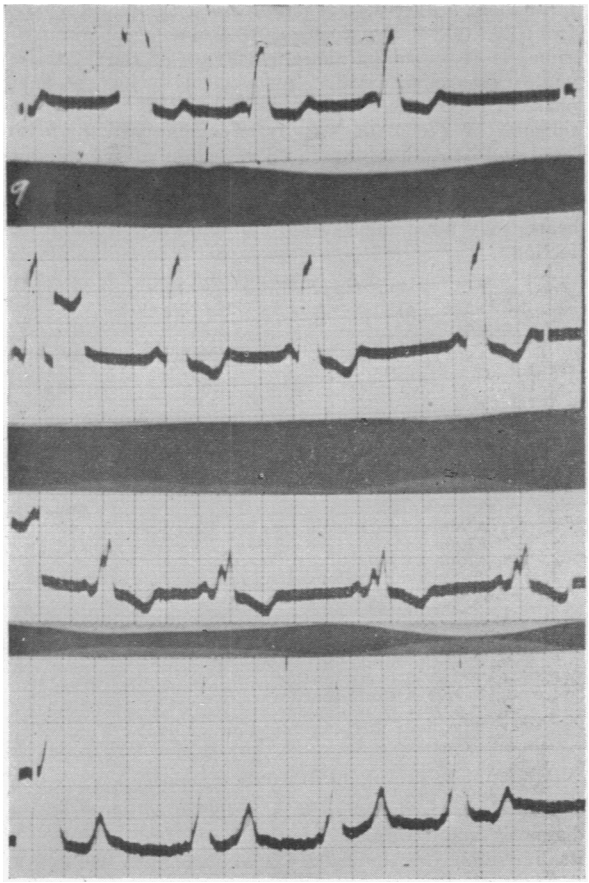

Fig. 7.—Short P-R with Wide QRS Complex.

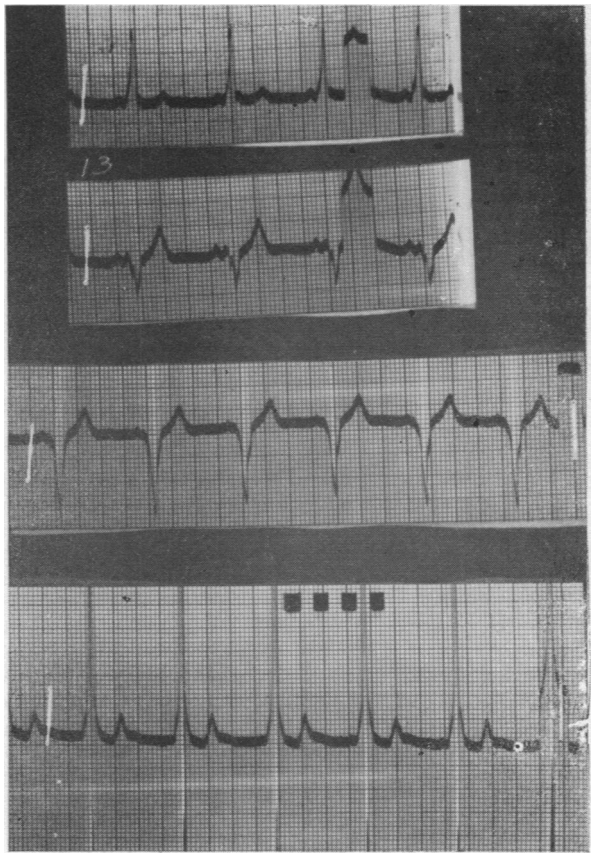

Fig. 8.—Short P-R with Wide QRS Complex.

suggests the possibility that rheumatic fever through its ability to interfere with conduction through the normal pathway may be capable of producing this type of abnormality in individuals in whose hearts such an aberrant conduction bundle exists. This supposition is in part supported by observation of one patient whose electrocardiographic pattern showed a tendency to shift from the normal to the abnormal type at various stages of rheumatic activity. This possibility is under further investigation.

THE ELECTRICAL AXIS

Deviation of the electrical axis to the left was noted in 318 patients and right axis deviation in 85 patients. Since this is within the limits of normal for individuals in this age group, no particular significance can be attached to this type of change. Variations in the electrical axis in subsequent tracings were rarely noted and never marked.

QRS COMPLEX

Other changes in the QRS complex are listed in Table IV. Only gross changes of the types enumerated were believed to be sufficiently significant to warrant inclusion in the table. They were found to occur in an insignificant proportion of the total studied. The presence of a deep Q wave in lead III as observed by Pardee[9] was noted in eight instances. Low voltage of QRS was observed in fourteen cases and is probably of some significance in patients in this age group. Slurring, notching and splintering of the QRS complex to a significant degree were of relatively infrequent occurrence.

ST JUNCTION

Abnormal displacement of the ST junction has been observed to be one of the commonest findings in acute rheumatic fever.[4] This is particularly true in the presence of acute pericarditis when the ST junction may be elevated in all leads with gradual return to the isoelectric line in conjunction with gradual inversion of the T waves.[10] In our series, abnormal displacement of the ST junction was noted in 74 patients (1.23 per cent) as listed in Table 5. In rare instances was the succession of changes noted by Bellet and McMillan[10] observed, although many instances of clinical acute pericarditis occurred among our patients. On the contrary in almost all of our patients in this group the deviation of the ST junction showed a tendency to constant displacement and rarely returned to normal. Since displacement of the ST junction has been shown to occur in at least as high a proportion of normal young adults as in those observed by us, the significance of this finding in the absence of other abnormalities seems doubtful. A fixed deviation of the ST junction, in the absence of T wave changes or other abnormalities does not appear to be of particular significance, at least in the present study. Other electrocardiographic changes associated with abnormalities of the ST junction are also noted in the table. In these patients at least, it seems likely that the associated changes are more significant than the deviations of the ST junction.

TABLE 4.—*QRS-Changes*

	Patients
1. Left Axis Deviation	318
2. Right Axis Deviation	85
3. QRS Low Voltage	14
4. Q-1 Deep	1
5. Q-2 Deep	2
6. Q-3 Deep	8
7. R-4 Absent	1
8. QRS Slurred, Notched, Splintered	11

TABLE 5.—*ST-Junction Abnormalities*

74 Patients (1.23%)		
Lead	Elevated	Depressed
I	14	3
II	48	5
III	23	6
IV	13	2
ST Changes with Prolonged PR-Interval		24
ST Changes with Prolonged PR-Interval and Abnormal T Waves		5
ST Changes with Abnormal T Waves		23

T WAVES

The presence of T wave abnormalities has been noted in from 3 to 40 per cent of all patients with rheumatic fever.[4] Pardee[8] states that if frequent serial tracings are recorded during the acute phase of rheumatic activity, as many as 60 per cent of all cases will be found to show inversion or some other abnormality of the T wave. Of our patients 125 (2.08 per cent) showed the T wave abnormalities listed in Table VI. Changes in T_3 alone when not associated with T wave abnormalities in other leads, were not considered significant and were not included in the table. It was believed to be of some value and interest to note the correlation of T wave changes in the various leads as listed in Table VII. Examples of some of the changes observed are seen in Figures 9, 10, 11, 12 and 13. Successive tracings on individual patients showed variations in this pattern and all these are included in the table. It is noted that changes in T_4 alone were most common, changes in T_2 and T_3 next in order of frequency and T wave changes in all four leads next in order of incidence. It has been previously observed that the succession of changes noted by Bellet and McMillan in cases of acute pericarditis were rarely observed among our patients. While the T wave abnormalities changed in successive tracings they did not necessarily revert to normal even upon complete subsidence of the acute rheumatic infection. Curiously, relatively few of those with persistent T wave abnormalities displayed any evidence of clinical heart disease. For example the patient from whom the tracing in Figure 13 was obtained was entirely quiescent by all clinical and laboratory criteria. Physical examination of the heart was entirely normal. However, he continued to display the same abnormality with but slight variation throughout a long period of observation. Upon discharge from treatment the electrocardiogram was about the same. It is suggested that alterations in the T waves, while evidence of cardiac involvement during the acute phase of rheumatic fever, cannot be used to estimate continuance of rheumatic activity. The observation of isolated and often long continued inversion of T_4 suggests the possibility that the finding of this type of abnormality in apparently healthy individuals with normal hearts may be an indication of antecedent rheumatic infection.

TABLE 6.—*T-Wave Changes*
125 Patients (2.08%)—268 Tracings

Lead	Low	Diphasic	Inverted
I	47	18	15
II	38	36	36
III	21	14	56
IV	26	37	52

TABLE 7.—*Association of T-Wave Abnormalities*

	Tracings
1. T-1 Alone	10
2. T-2 Alone	79
3. T-4 Alone	79
4. T-1, T-2 Combination	9
5. T-1, T-3 Combination	1
6. T-1, T-4 Combination	17
7. T-2, T-3 Combination	64
8. T-2, T-4 Combination	5
9. T-3, T-4 Combination	1
10. T-1, T-2, T-3 Combination	13
11. T-2, T-3, T-4 Combination	8
12. T-1, T-2, T-4 Combination	5
13. T-1, T-2, T-3, T-4 Combination	45

DISCUSSION

The electrocardiogram is a valuable adjunct in the diagnosis and treatment of rheumatic fever. However, its limitations are indicated by some of the findings in the present study. While prolongation of the P-R interval is a very significant observation in the diagnosis of rheumatic fever in suspected cases, as an isolated finding its significance is in doubt. Furthermore, as a guide to activity of the rheumatic process, its value is also

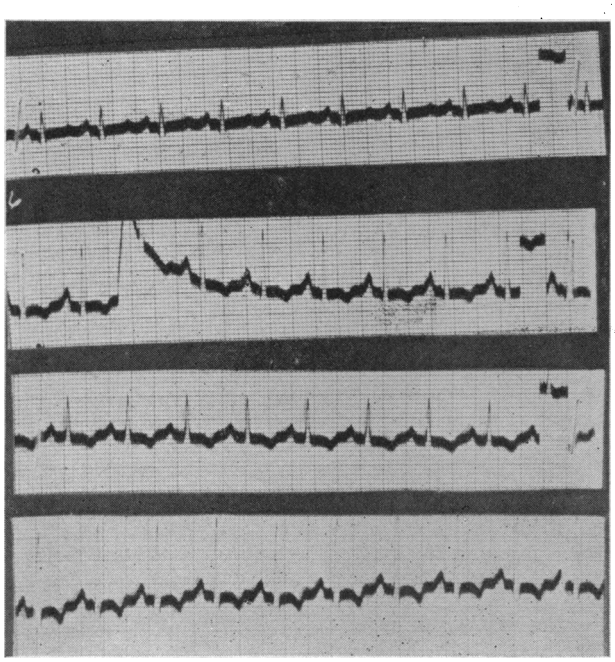

Fig. 9.—Inversion of T_2, T_3 and T_4.

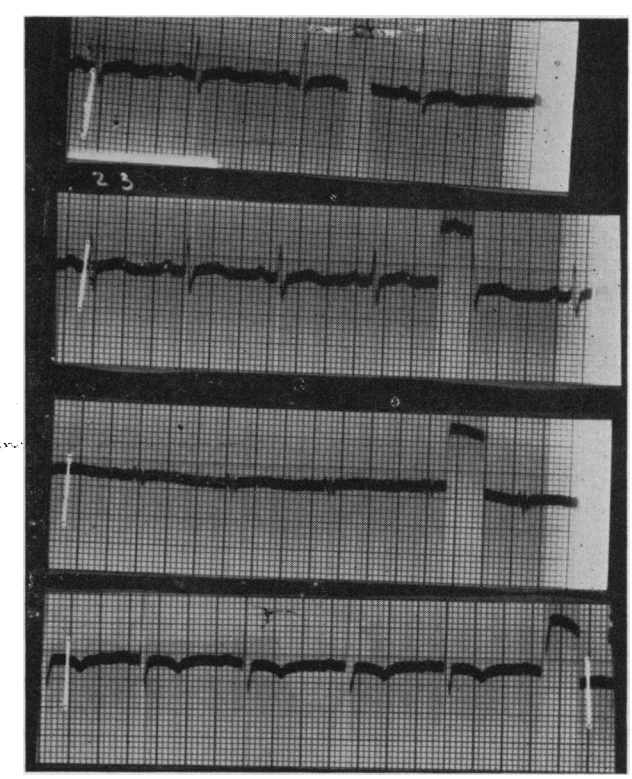

Fig. 10.—Diphastic T_1, T_4 Inverted.

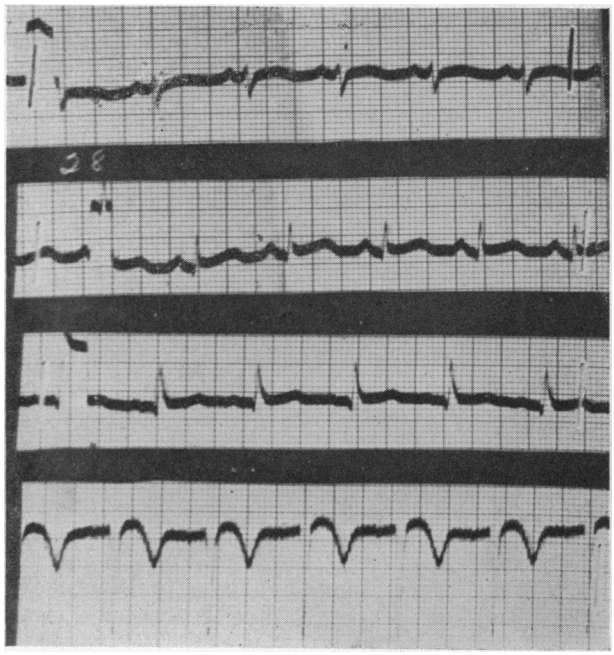

Fig. 11.—Absent R_4, T_4 Deeply Inverted.

limited and requires interpretation in the light of other findings and the overall clinical picture. T wave abnormalities are probably of greater diagnostic importance. Particularly in the age group under consideration, in whom arteriosclerotic disease of the coronary arteries is relatively infrequent, T wave changes may be of great significance. A possible explanation for the T wave abnormalities observed in rheumatic fever is supplied by the frequency with which changes in the coronary arteries have been noted in those of our patients who died during the course of rheumatic fever. In every such case studied at autopsy, coronary angititis was an outstanding pathological finding. Two patients died of thrombosis of major coronary vessels previously damaged by rheumatic arteritis. The almost universal involvement of the coronary vessels in rheumatic fever certainly provides ample explanation for the T wave changes which are so reminiscent of those noted in other forms of coronary artery disease. Damage to more than one part of the coronary circulation seems indicated by the changes observed.

From the standpoint of determination of rheumatic activity, however, the importance of T wave alterations must be evaluated in conjunction with other clinical and laboratory findings. All other electrocardiographic changes observed are in no way peculiar to rheumatic fever, and should be evaluated with this in view.

SUMMARY

1. The electrocardiographic abnormalities observed in 6,000 cases of rheumatic fever are noted.

2. The significance of certain arrhythmias is indicated. It is suggested that heightened nodal irritability exists in certain cases of rheumatic fever.

3. The significance of alterations in the P waves, particularly when changing is observed.

4. The limitation of the diagnostic and prognostic importance of prolongation of the P-R interval is noted. Both prolonged and changing P-R intervals were observed in apparently inactive rheumatic fever patients.

5. The possible rheumatic etiology of certain instances of bundle branch block and the syndrome of short P-R interval with wide QRS complex in certain instances is observed.

6. Deviation of the ST junction, when fixed and un-

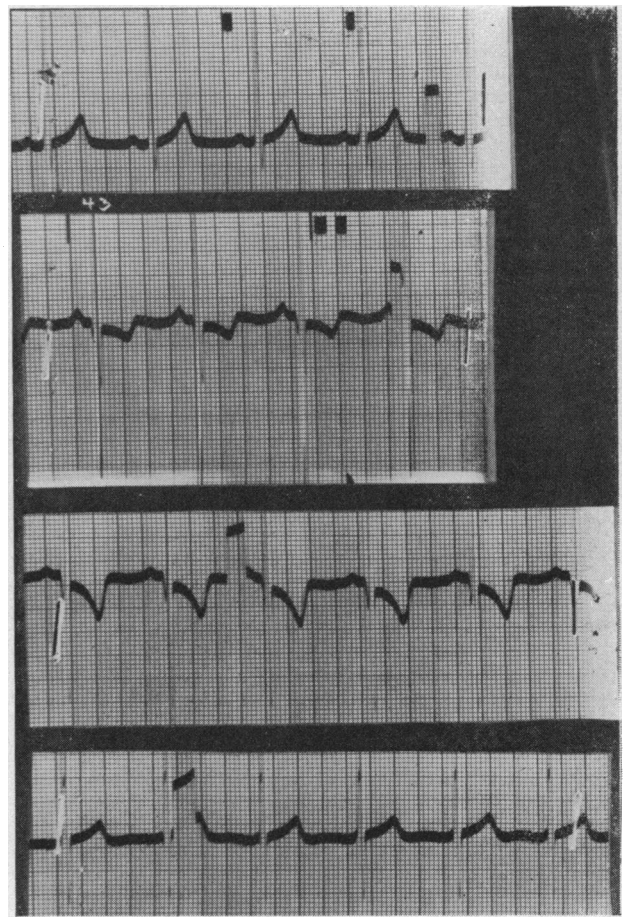

Fig. 12—ST_2 and ST_3 Depressed, T_2 and T_3 Inverted.

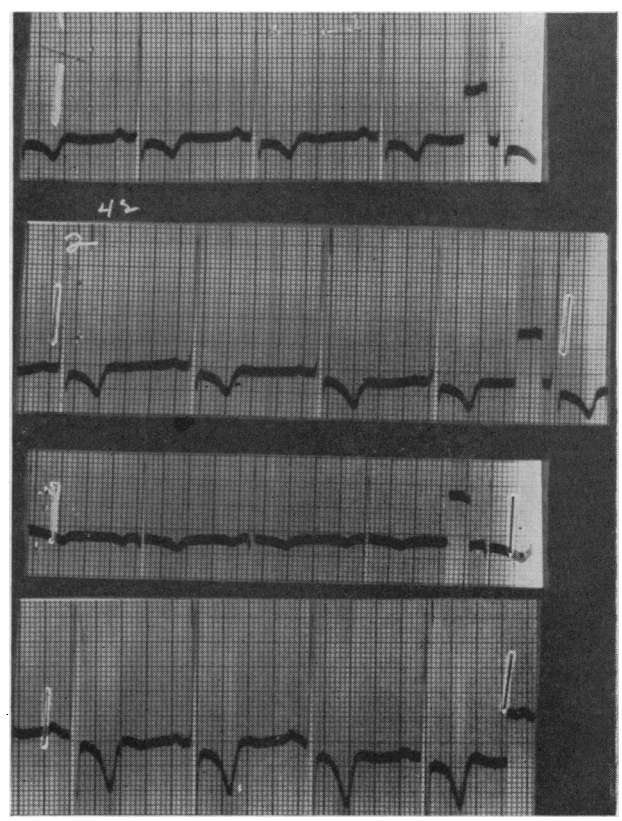

Fig. 13.—ST_1, ST_2 and ST_4 Depressed. T Inverted in All Leads.

associated with other abnormalities was not observed to a greater degree than in normal individuals. It is believed to be without significance.

7. Frequent changes in T waves were observed in this group. The limitation of the value of T wave changes in the estimation of rheumatic activity is noted. An explanation for these changes based on changes in the coronary circulation is suggested.

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TULAREMIC PNEUMONIA*

REPORT OF A FATAL CASE

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TULAREMIA (deer fly fever) is an infectious disease caused by Bacterium tularense (Pasteurella tularensis), occurring in humans and over twenty kinds of wild life, especially in wild rabbits and hares. It was first discovered by McCoy[1] in 1910. The original investigative work was conducted in Tulare County, California, hence the name tularemia.

Man becomes infected by contact of his unprotected, even apparently unbroken skin or mucus membranes, with raw tissue of infected animals, and by bites of blood sucking ticks and flies which have fed on infected animals.[2] Mosquitoes have been reported capable of transmitting the disease to man.[3] Whether or not humans may contract the disease via the respiratory tract is an unsettled question, the proponents and opponents both having evidence worthy of being weighed.[4]

Tularemia has been considered to be almost exclusively of the following four types: 1. Ulceroglandular; 2. Oculoglandular; 3. Glandular; and 4. Typhoidal, or cryptogenic.

While the pulmonary form has been known it, until recently, was considered to be exceedingly rare.

TULAREMIC PNEUMONIA

The marked increase in the number of cases of tularemic pneumonia being reported in the last several years indicates among other things the systemic nature of tularemic infections. Blackford and Casey,[5] in 1941, were able to find but 150 reported cases of tularemic pneumonia in the American literature. Stuart and Pullen,[4] in August, 1945, increased this figure to 268. This figure includes cases which seem almost purely pneumonia and those which have pneumonia as part of a more systemic or generalized tularemia. They found tularemic pneumonia in 9.3 per cent of a series of 225 cases of tularemia. The cases of relatively pure pneumonia may be difficult to separate accurately from those having pneumonia as a part of a cryptogenic tularemia. The relatively pure cases of tularemic pneumonia still are to be considered rare. It is felt that the case being reported is such a case. This article with a case report is submitted for various reasons: tularemic pneumonia is still somewhat of a curiosity; tularemic pneumonias still have a high mortality; streptomycin gives encouraging promise of being the most effective therapeutic agent yet employed; and, unless this condition is kept in mind and included in the differential diagnosis in pneumonic conditions, these cases will be incorrectly diagnosed and incorrectly treated, a fatal issue likely resulting.

The first published report of pleuropulmonary tularemia was probably that of Verbrycke[6] in 1924. Sante[7] described the roentgenographic findings of pleuropulmonary tularemia in 1931. The non-typhoidal cases usually present early hilar adenopathy with subsequent retrograde extension of the involvement through lymphatic channels to the lung parenchyma or even the pleura. The typhoidal cases usually present primary involvement of the lung parenchyma. Lung abscess, pneumothorax, pleural effusion, and residual fibrosis have been reported.

PATHOLOGY

Gross and microscopic features were described in detail by Blackford and Casey.[5] The most frequent finding is a lobular pneumonia involving any or all lobes. Both red and gray hepatization are frequently found.

DIAGNOSIS

Moss and Weilbaecher,[8] in 1941, reviewed the recent advances in the diagnosis of tularemia.

An occupational history may expose a clue to the diagnosis. A history of the patient's having been exposed to ticks, deer flies, or having been on a hunting or camping trip may be illuminating.

The symptoms vary greatly in severity. Frequently they are so mild that, without the chest film pneumonia would not be recognized. Especially in those cases seeming to develop as a primary pneumonia, suggesting that the organisms may have been inhaled, the onset may be sudden and the course fulminating. Cough, fever, chill, diaphoresis, pleurisy, sputum, dyspnea, and prostration are common. Cyanosis, delirium, stupor, and coma may develop in severe cases.

The fever is usually irregular and spiking, the pulse relatively slow.

In general, the physical findings are usually those to be expected in atypical pneumonia, but occasionally may be those of lobar pneumonia. The physical findings may be normal, while the chest film discloses the presence of pneumonia.

Special Studies.—The x-ray findings were described above. Sputum studies have, at times, yielded the organism. Blood cultures, though not frequently fruitful, should be taken. Agglutination tests, especially if there is a rising titre, are more valuable but cannot be relied upon until the second week of the illness. In some cases, more especially the fulminating ones, the test may be delayed or fail to develop.

Animal inoculation with properly collected material from the lung, lymph nodes, blood and sputum gives a high percentage of accurate results. Tissues from the spleen, liver, lymph nodes, and lung taken at the time of autopsy may be injected into susceptible animals for diagnostic purposes.

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